

## L-Methylfolate 7.5 mg Tablets

## L-Methylfolate 15 mg Tablets

### DESCRIPTION

L-Methylfolate Tablets are a medical food for the dietary management of conditions relating to sub-optimal L-methylfolate levels, recommended for use under the supervision of a physician or healthcare provider.

Each **L-Methylfolate 7.5 mg** tablet contains 7.5 mg of L-methylfolate (Metafolin®)\*.

\*CAS#151533-22-1

Each **L-Methylfolate 15 mg** tablet contains 15 mg of L-methylfolate (Metafolin®)\*.

\*CAS#151533-22-1

### L-Methylfolate 7.5 mg Other Ingredients:

Dibasic Calcium Phosphate Dihydrate, Silicified Microcrystalline Celluloses, Opadry II Blue 85F90748 [color] (Polyvinyl Alcohol, Titanium Dioxide [color], PEG 3350, Talc, FD&C Blue No. 2 Aluminum Lake [color]), Magnesium Stearate (Vegetable Grade), and Carnauba Wax.

**L-Methylfolate 7.5 mg** tablets do not contain sugar, lactose, yeast or gluten.

### L-Methylfolate 15 mg Other Ingredients:

Dibasic Calcium Phosphate Dihydrate, Silicified Microcrystalline Cellulose, Opadry II Orange 85F43102 [color] (Polyvinyl Alcohol, PEG 3350, Talc, Titanium Dioxide [color], FD&C Yellow No. 6\* Aluminum Lake [color], FD&C Yellow No. 5\*\* Aluminum Lake [color], FD&C Red No. 40 Aluminum Lake [color], FD&C Blue No. 2 Aluminum Lake [color]), Magnesium Stearate (Vegetable Grade), and Caruba Wax.

**L-Methylfolate 15 mg** tablets do not contain sugar, lactose, yeast or gluten.

\*Contains FD&C Yellow No. 6 as a color additive

\*\*Contains FD&C Yellow No. 5 (Tartrazine) as a color additive (see **PRECAUTIONS**).

**L-Methylfolate** is labeled as a medical food for use under the active and ongoing medical supervision of a physician or health-care provider on a recurring basis for, among other things, instructions on their use.

Medical foods are designed for the dietary management of a patient who, because of therapeutic or chronic medical needs, has limited or impaired capacity to ingest, digest, absorb or metabolize ordinary foodstuffs or certain nutrients, or who has other special medically determined nutrient requirements, the dietary management of which cannot be achieved by the modification of the normal diet alone.<sup>1</sup> This Medical Food is not subject to NDA or ANDA approval and is not an Orange Book product. Although FDA does not require a prescription for Medical Foods, this product is intended to be used under active medical supervision. This product is not eligible for government reimbursement under federal programs, but is eligible for reimbursement under state programs on a case-by-case basis. Please check with a specific state to determine proper reimbursement eligibility.

**These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

### CLINICAL PHARMACOLOGY

**L-Methylfolate** is a medical food, which consists of a proprietary biologically active folate, derived from food sources.

### INDICATIONS AND USAGE

L-Methylfolate Tablets are labeled as a medical food for the distinct nutritional requirements of individuals who have or are at risk for hyperhomocysteinemia and other conditions relating to suboptimal L-methylfolate levels.

### CONTRAINDICATIONS

**L-Methylfolate** is contraindicated in patients with known hypersensitivity to any of the components contained in this product.

### PRECAUTIONS

This product contains FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin sensitivity.

### General:

Folic acid, when administered in daily doses above 0.1 mg, may obscure the detection of B<sub>12</sub> deficiency (specifically, the administration of folic acid may reverse the hematological manifestations of B<sub>12</sub> deficiency, including pernicious anemia, while not addressing the neurological manifestations). L-methylfolate may be less likely than folic acid to mask vitamin B<sub>12</sub> deficiency.<sup>2,3</sup> Folate therapy alone is inadequate for the treatment of a B<sub>12</sub> deficiency.

### Patient Information:

**L-Methylfolate is a medical food<sup>1</sup> for use under the medical supervision of a physician or health-care provider.**

**Interaction with Drugs:** Before using this product, tell your doctor or pharmacist of all the products you use. Keep a list of all your medications with you, and share the list with your doctor and pharmacist. No decrease in effectiveness of drugs has been reported with the use of L-Methylfolate.

L-Methylfolate contains folate, which may have interactions with the following:

- Antiepileptic drugs (AED): The AED class including, but not limited to, phenytoin, carbamazepine, primidone, valproic acid, phenobarbital and lamotrigine have been shown to impair folate absorption and increase the metabolism of circulating folate. Additionally,

concurrent use of folic acid has been associated with enhanced phenytoin metabolism, lowering the level of this AED in the blood and allowing break through seizures to occur.<sup>4,5,7,10</sup>

- Capecitabine: Folinic acid (5-formyltetrahydrofolate) may increase the toxicity of Capecitabine.<sup>6</sup>
- Dihydrofolate Reductase Inhibitors (DHFRi): DHFRi block the conversion of folic acid to its active forms, and lower plasma and red blood cell folate levels. DHFRi include aminopterin, methotrexate, pyrimethamine, triamterene, and trimethoprim.<sup>7</sup>
- Fluoxetine: Fluoxetine extends a non-competitive inhibition of the 5-methyltetrahydrofolate active transport in the intestine.<sup>8</sup>
- Isotretinoin: Reduced folate levels have occurred in some patients taking isotretinoin.<sup>9</sup>
- Nonsteroidal Anti-inflammatory Drugs (NSAIDs): NSAIDs have been shown to inhibit some folate dependent enzymes in laboratory experiments NSAIDs include ibuprofen, naproxen, indomethacin and sulindac.<sup>7</sup>
- Oral Contraceptives: Serum folate levels may be depressed by oral contraceptive therapy.<sup>7</sup>
- Methylprednisolone: Reduced serum folate levels have been noted after treatment with methylprednisolone.<sup>7</sup>
- Pancreatic Enzymes: Reduced folate levels have occurred in some patients taking pancreatic extracts.<sup>7</sup>
- Pentamidine: Reduced folate levels have been seen with prolonged intravenous pentamidine.<sup>7</sup>
- Metformin treatment in patients with type 2 diabetes decreases serum folate.<sup>11,12</sup>
- Warfarin can produce significant impairment in folate status after a 6-month therapy.<sup>13</sup>

### ADVERSE REACTIONS

Allergic reactions have been reported following the use of oral L-methylfolate.

**Keep this and all medications out of the reach of children. In case of accidental overdose, seek professional assistance or contact a poison control center immediately.**

### DOSAGE AND ADMINISTRATION

The usual adult dose is 7.5 mg to 15 mg given daily with or without food or as directed under medical supervision.

### HOW SUPPLIED

**L-Methylfolate is a medical food for use under the supervision of a physician or health-care provider.**

**L-Methylfolate 7.5 mg** is a round light-blue tablet, imprinted with "LMF" on one side and "7.5" on the other side.

Bottles of 30 Product Code 51991-808-33† Use under medical/physician supervision.

Bottles of 90 Product Code 51991-808-90‡ Use under medical/physician supervision.

**L-Methylfolate 15 mg** is an orange oval-coated tablet, imprinted with "LMF" on one side and "15" on the other side.

Bottles of 90 Product Code 51991-809-90‡ Use under medical/physician supervision.

†Breckenridge Pharmaceutical, Inc. does not represent these product codes to the National Drug Codes (NDC). Product codes are formatted according to standard industry practice, to meet the formatting requirements of pharmacy and health insurance computer systems.

### Storage:

Store at 25°C (77°F), excursions permitted 15°C to 30°C (59°F to 86°F) See USP Controlled Room Temperature. Protect from light and moisture.

### PATENTS

For information on applicable patents, please visit [www.bpirx.com](http://www.bpirx.com)

### REFERENCES

1. United States Food and Drug Administration Title 21 Code of Federal Regulations 101.9(j) (8).
  2. Akoglu B et al. Euro J Clin Nutrition. 2007;1-6.
  3. Scott JM and Weir DG. The Lancet. 1981;2:337-40.
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  5. Morrell M. Curr. 2002; 2(2):31-34.
  6. Capecitabine Package Insert; Roche Laboratories, 2000
  7. Natural Standard Research Collaboration (NIH). Folate (folic acid) Monograph 2009
  8. Amiburu A, et al. J. Physiol. Biochem., 57 (2), 71-80, 2001
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  11. Wulfelle MG, et al. Journal of Internal Medicine. 2003; 254: 455- 463.
  12. Desouza C, et al. Drugs 2002; 62(4): 605-16.
  13. Sobczynska-Malefora A et al. Blood Coagul Fibrinolysis 2009 Jun;20(4):297-302
- Metafolin® is a registered trademark of Merck KGaA, Darmstadt, Germany.

**To report a serious adverse event contact: 1-800-367-3395**

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